PATENT COOPERATION TREATY

From	the RNATIONAL SEA	ARCHING ALITH	ORITY		REC'D 18 AUG 2005
To:	<u> </u>				PCT PCT
	see form	PCT/ISA/220		INTERNATION Date of mailing	TTEN OPINION OF THE DNAL SEARCHING AUTHORITY (PCT Rule, 43 <i>bis</i> .1)
• •	icant's or agent's file form PCT/ISA/2:			FOR FURTHER See paragraph 2 be	
_	national application l T/EP2005/00056		International filing date (c 18.01.2005	day/month/year)	Priority date (day/month/year) 22.01.2004
		• •	both national classification (72, C12Q1/68, A61K3		
Appli AKZ	icant ZO NOBEL N.V.		·		
1.	Box No. I Box No. II Box No. III Box No. IV Box No. V Box No. V Box No. VI Box No. VIII Box No. VIII FURTHER ACTION If a demand for it written opinion of the applicant cho	Basis of the open Priority Non-establishme Lack of unity of Reasoned state applicability; cit Certain docume Certain defects Certain observational prelif the International prelification of the Internation of the Int	nent of opinion with regard invention sement under Rule 43 bistations and explanations ents cited in the international applations on the international inter	ard to novelty, invention (a)(i) with regard to supporting such station al application when the IPEA and the learning the	lll usually be considered to be a However, this does not apply where e chosen IPEA has notifed the
	will not be so con If this opinion is, submit to the IPE months from the whichever expire For further option	nsidered. as provided about A a written reply date of mailing ones later. as, see Form PC	ve, considered to be a work together, where approposed Form PCT/ISA/220 or the T/ISA/220.	vritten opinion of the oriate, with amendm	ational Searching Authority IPEA, the applicant is invited to lents, before the expiration of three in of 22 months from the priority date,
3.	For further details	s, see notes to F	orm PCT/ISA/220.		

Name and mailing address of the ISA:

Authorized Officer



European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016

Hix, R

Telephone No. +31 70 340-3898



International application No. PCT/EP2005/000562

Box No. I Basis of the opinion	-
1. With regard to the language, this opinion has been established on the basis of the international application the language in which it was filed, unless otherwise indicated under this item.	in
This opinion has been established on the basis of a translation from the original language into the follow language, which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).	wing
2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:	
a. type of material:	
🖾 a sequence listing	
☐ table(s) related to the sequence listing	
b. format of material:	
in computer readable form	
c. time of filing/furnishing:	•
□ contained in the international application as filed.	
☐ filed together with the international application in computer readable form.	
☐ furnished subsequently to this Authority for the purposes of search.	
3. In addition, in the case that more than one version or copy of a sequence listing and/or table relating the has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.	reto
4. Additional comments:	

International application No. PCT/EP2005/000562

_								
_	Box I	No. IV Lack of ur	nity of invention	n				
1.		response to the in	vitation (Form F	PCT/ISA/20	06) to pay additional fees, the applicant has:			
		☐ paid addition	al fees.					
		☐ paid addition	al fees under pi	otest.				
		☐ not paid add	itional fees.	· .	•			
2.		his Authority found e applicant to pay		ment of u	nity of invention is not complied with and chose not to invite			
3.	This A	uthority considers	that the requirer	ment of un	ity of invention in accordance with Rule 13.1, 13.2 and 13.3 is			
	🗆 соі	nplied with						
	⊠ not	complied with for t	he following rea	isons:				
	S	ee separate sheet						
4.	Conse	Consequently, this report has been established in respect of the following parts of the international application:						
	□ all	parts.						
	the	parts relating to cla	aims Nos. 1, 10	-14, 23-32				
				·				
	Box N indus				3bis.1(a)(i) with regard to novelty, Inventive step or one supporting such statement			
1.	Staten	nent						
	Novelt	y (N)	Yes: No:	Claims Claims	1, 10-14, 23-32			
	Invent	ve step (IS)	Yes: No:	Claims Claims	1, 10-14, 23-32			
	Indust	rial applicability (IA)	Yes: No:	Claims Claims	1, 10-14, 23-32			
2	Citatio	ns and explanation	s					

see separate sheet

International application No.

PCT/EP2005/000562

Re Item IV

Lack of unity of invention

The separate inventions/groups of invention are:

Invention 1: Claims 1 and 14 completely and claims 10 to 13, 23 to 32 partially.

Nucleic acid sequence encoding a 75kD *Lawsonia intracellularis* protein or a part of said nucleic acid sequence that encodes an immunogenic fragment of said protein said nucleic acid sequence, or said part thereof having at least 90% homology with the nucleic acid sequence as depicted in SEQ ID NO: 1, protein that is at least 90% homologous to SEQ ID NO: 2, live recombinant carrier, host cell, vaccine comprising said nucleic acid, use of said protein in the manufacture of a vaccine and method of preparing said vaccine, diagnostic tests involving said nucleic acid or proteins.

Invention 2: Claims 2 and 15 completely and claims 10 to 13, 23 to 32 partially.

Nucleic acid sequence encoding a 27kD Lawsonia intracellularis protein or a part of said nucleic acid sequence that encodes an immunogenic fragment of said protein said nucleic acid sequence, or said part thereof having at least 90% homology with the nucleic acid sequence as depicted in SEQ ID NO: 3, protein that is at least 90% homologous to SEQ ID NO: 4, live recombinant carrier, host cell, vaccine comprising said nucleic acid, use of said protein in the manufacture of a vaccine and method of preparing said vaccine, diagnostic tests involving said nucleic acid or proteins.

Invention 3: Claims 3 and 16 completely and claims 10 to 13, 23 to 32 partially. Nucleic acid sequence encoding a 62kD Lawsonia intracellularis protein or a part of said nucleic acid sequence that encodes an immunogenic fragment of said protein said nucleic acid sequence, or said part thereof having at least 90% homology with the nucleic acid sequence as depicted in SEQ ID NO: 5, protein that is at least 90% homologous to SEQ ID NO: 6, live recombinant carrier, host cell, vaccine comprising said nucleic acid, use of said protein in the manufacture of a vaccine and method of preparing said vaccine, diagnostic tests involving said nucleic acid or proteins.

Invention 4: Claims 4 and 17 completely and claims 10 to 13, 23 to 32 partially.

Nucleic acid sequence encoding a 57kD Lawsonia intracellularis protein or a part of said nucleic acid sequence that encodes an immunogenic fragment of said protein said nucleic

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acid sequence, or said part thereof having at least 90% homology with the nucleic acid sequence as depicted in SEQ ID NO: 7, protein that is at least 90% homologous to SEQ ID NO: 8, live recombinant carrier, host cell, vaccine comprising said nucleic acid, use of said protein in the manufacture of a vaccine and method of preparing said vaccine, diagnostic tests involving said nucleic acid or proteins.

Invention 5: Claims 5 and 18 completely and claims 10 to 13, 23 to 32 partially. Nucleic acid sequence encoding a 74kD Lawsonia intracellularis protein or a part of said nucleic acid sequence that encodes an immunogenic fragment of said protein said nucleic acid sequence, or said part thereof having at least 90% homology with the nucleic acid sequence as depicted in SEQ ID NO: 9, protein that is at least 90% homologous to SEQ ID NO: 10, live recombinant carrier, host cell, vaccine comprising said nucleic acid, use of said protein in the manufacture of a vaccine and method of preparing said vaccine, diagnostic tests involving said nucleic acid or proteins.

Invention 6: Claims 6 and 19 completely and claims 10 to 13, 23 to 32 partially. Nucleic acid sequence encoding a 44kD *Lawsonia intracellularis* protein or a part of said nucleic acid sequence that encodes an immunogenic fragment of said protein said nucleic acid sequence, or said part thereof having at least 90% homology with the nucleic acid sequence as depicted in SEQ ID NO: 11, protein that is at least 90% homologous to SEQ ID NO: 12, live recombinant carrier, host cell, vaccine comprising said nucleic acid, use of said protein in the manufacture of a vaccine and method of preparing said vaccine, diagnostic tests involving said nucleic acid or proteins.

Invention 7: Claims 7 and 20 completely and claims 10 to 13, 23 to 32 partially. Nucleic acid sequence encoding a 43kD *Lawsonia intracellularis* protein or a part of said nucleic acid sequence that encodes an immunogenic fragment of said protein said nucleic acid sequence, or said part thereof having at least 90% homology with the nucleic acid sequence as depicted in SEQ ID NO: 13, protein that is at least 90% homologous to SEQ ID NO: 14, live recombinant carrier, host cell, vaccine comprising said nucleic acid, use of said protein in the manufacture of a vaccine and method of preparing said vaccine, diagnostic tests involving said nucleic acid or proteins.

Invention 8: Claims 8 and 21 completely and claims 10 to 13, 23 to 32 partially.

Nucleic acid sequence encoding a 26/31kD Lawsonia intracellularis protein or a part of said nucleic acid sequence that encodes an immunogenic fragment of said protein said nucleic acid sequence, or said part thereof having at least 90% homology with the nucleic acid sequence as depicted in SEQ ID NO: 15, protein that is at least 90% homologous to SEQ ID NO: 16, live recombinant carrier, host cell, vaccine comprising said nucleic acid, use of said protein in the manufacture of a vaccine and method of preparing said vaccine, diagnostic tests involving said nucleic acid or proteins.

Invention 9: Claims 9 and 22 completely and claims 10 to 13, 23 to 32 partially. Nucleic acid sequence encoding a 101kD Lawsonia intracellularis protein or a part of said nucleic acid sequence that encodes an immunogenic fragment of said protein said nucleic acid sequence, or said part thereof having at least 90% homology with the nucleic acid sequence as depicted in SEQ ID NO: 17, protein that is at least 90% homologous to SEQ ID NO: 18, live recombinant carrier, host cell, vaccine comprising said nucleic acid, use of said protein in the manufacture of a vaccine and method of preparing said vaccine, diagnostic tests involving said nucleic acid or proteins.

The general concept of characterizing nucleic acids which encode *Lawsonia intracellularis* proteins as using them in vaccines against *Lawsonia intracellularis* is already known from the prior art document D1: EP-A-1 219 711 (Akzo Nobel N.V.) and D2: WO-A-0 226 250 (Arizona Board of Regents on behalf of the University of Arizona.)

D1 discloses nucleic acid sequences encoding *Lawsonia intracellularis* outer membrane proteins and immunogenic fragments for use as vaccines against *Lawsonia intracellularis*. D2 describes vaccines against proliferative ileitis containing protective immunogenic subunits of *Lawsonia intracellularis*.

Due to the fact that the common unifying concept is known in the state of the art, there appears therefore to be no technical features in common between the different inventions involving different nucleotide and amino acid sequences, that could provide a novel and inventive unifying concept.

Consequently, the requisite unity of invention (Rule 13.1 PCT) therefore

no longer exists inasmuch as a technical relationship involving one or more of the same or corresponding special technical features in the sense of Rule 13.2 PCT does not exist between the subject-matter of the groups of claims.

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Examination of:

Invention 1: Claims 1 and 14 completely and claims 10 to 13, 23 to 32 partially.

Nucleic acid sequence encoding a 75kD Lawsonia intracellularis protein or a part of said nucleic acid sequence that encodes an immunogenic fragment of said protein said nucleic acid sequence, or said part thereof having at least 90% homology with the nucleic acid sequence as depicted in SEQ ID NO: 1, protein that is at least 90% homologous to SEQ ID NO: 2, live recombinant carrier, host cell, vaccine comprising said nucleic acid, use of said protein in the manufacture of a vaccine and method of preparing said vaccine, diagnostic tests involving said nucleic acid or proteins.

- The following documents are referred to in this communication; the numbering will be adhered to in the rest of the procedure:
 - D1: EP-A-1 219 711 (Akzo Nobel N.V.)

D2: WO-A-0 226 250 (Arizona Board of Regents on behalf of the University of Arizona.)

- 2 **NOVELTY** (Art. 33(2) PCT)
- In view of the prior art cited, claims 1 and 14 and claims dependent thereon appear to be novel and meet therefore the requirements of Art.33(2) PCT, since

the nucleic and amino acid sequences SEQ ID NOs: 1 and 2 are not disclosed in the state of the art.

3 **INVENTIVE STEP** (Art. 33(3) PCT)

- 3.1 Documents D2 and D3 are considered to represent the most relevant state of the art. D2 discloses nucleic acid sequences encoding *Lawsonia intracellularis* outer membrane proteins and immunogenic fragments for use as vaccines against *Lawsonia intracellularis*. D3 describes vaccines against proliferative ileitis containing protective immunogenic subunits of *Lawsonia intracellularis*.
- 3.2 The subject-matter of the present application and claims 1 and 14 and claims dependent thereon involve different nucleic acid sequences and their use as immunogenic fragments as vaccines against *Lawsonia intracellularis*.
- 3.3 The problem may be defined as the provision of alternative nucleic acid sequences and immunogenic fragments for use as vaccines against *Lawsonia intracellularis*.
- However due to the fact that the above problem has previously been solved by the subunit vaccines of the state of the art and that there is no evidence in the description that the nucleic or amino acid sequences SEQ ID NOs: 1 and 2 actually solve the problem through initiating an effective protective immune response to *Lawsonia intracellularis*, the subject-matter of claims 1 and 14 cannot be recognized as involving an inventive step according to Article 33(3) PCT.
- Dependent claims 10 to 13, 23 to 32, as far as they are dependent upon claims 1 and 14, do not appear to contain any additional features which, in combination with the features of any claim to which they refer, involve an inventive step.
- In view of the above, the present application does not meet the requirements of Article 33(3) PCT, because the subject-matter of claims 1, 10 to 14, 23 to 32 does

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not involve an inventive step.

For the assessment of the present claims 23 and 24 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

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From the INTERNAT	IONAL SEAF	RCHING AUTH	ORITY		WIPO	AUG 2005
To:		<u> </u>		•	PCT	PCT
·	see form F	PCT/ISA/220		INTERNATIO	TEN OPINION OF NAL SEARCHING PCT Rule 43 <i>bis</i> .1)	_
		· .		Date of mailing (day/month/year) se	e form PCT/ISA/210 (se∞no	i sheet)
	or agent's file i			FOR FURTHER A		-
PCT/EP2	al application N 005/000562	· ·	International filing date (date)		Priority date (day/monthly 22.01.2004	ear)
C07K14/			both national classification /12, C12Q1/68, A61K3			
Applicant AKZO NO	OBEL N.V.					
	Box No. I Box No. II Box No. IV Box No. V Box No. VI Box No. VII Box No. VIII	Basis of the operation	nent of opinion with regard Invention Tement under Rule 43 <i>bi</i> s Stations and explanations	ard to novelty, inventions. 5.1(a)(i) with regard to supporting such states to the states are t	ve step and industrial app novelty, inventive step or tement	
if a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1 bis(b) that written opinions of this International Searching Authority will not be so considered. If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later. For further options, see Form PCT/ISA/220.						
3. For	further detail	s, see notes to	Form PCT/ISA/220.			
Name and	mailing addres	ss of the ISA:		Authorized Officer		selles Petentes



European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016

Hix, R

Telephone No. +31 70 340-3898



International application No. PCT/EP2005/000562

_	Box	o. I Basis of the opinion
1.		gard to the language, this opinion has been established on the basis of the international application in guage in which it was filed, unless otherwise indicated under this item.
	la	is opinion has been established on the basis of a translation from the original language into the following guage , which is the language of a translation furnished for the purposes of international search ader Rules 12.3 and 23.1(b)).
2.	With neces	gard to any nucleotide and/or amino acid sequence disclosed in the international application and ary to the claimed invention, this opinion has been established on the basis of:
	a. typ	of material:
	\boxtimes	a sequence listing
		table(s) related to the sequence listing
	b. for	at of material:
	×	in written format
	×	in computer readable form
	c. tim	of filing/furnishing:
	\boxtimes	contained in the international application as filed.
	\boxtimes	filed together with the international application in computer readable form.
		furnished subsequently to this Authority for the purposes of search.
3.	h c	addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto been filed or furnished, the required statements that the information in the subsequent or additional bies is identical to that in the application as filed or does not go beyond the application as filed, as propriate, were furnished.
4.	Additi	nal comments:

International application No. PCT/EP2005/000562

	Во	x No. IV	Lack of unity of	inventio	1			
1.		☐ In response to the invitation (Form PCT/ISA/206) to pay additional fees, the applicant has:						
			paid additional fee	S.		•		
			paid additional fee	s under pr	otest.			
			not paid additional					
2.			uthority found that the plicant to pay addition		ment of un	nity of invention is not complied with and chose not to invite		
3.	Thi	s Autho	rity considers that th	e requirer	nent of uni	ity of invention in accordance with Rule 13.1, 13.2 and 13.3 is		
	□ complied with							
	\boxtimes	not com	plied with for the fol	lowing rea	isons:			
		see se	parate sheet					
4.	Coi	Consequently, this report has been established in respect of the following parts of the international application:						
	□ all parts.							
		•	s relating to claims I	Nos. 1, 10	-14, 23-32			
	—	are pero						
	Bo	x No. V lustrial a	Reasoned states	ment und	er Rule 43 explanatio	3bis.1(a)(i) with regard to novelty, inventive step or one supporting such statement		
1.	Sta	tement						
	No	velty (N)		Yes: No:	Claims Claims	1, 10-14, 23-32		
	Inv	entive st	tep (IS)	Yes: No:	Claims Claims	1, 10-14, 23-32		
	Ind	ustrial a	pplicability (IA)	Yes: No:	Claims Claims	1, 10-14, 23-32		

see separate sheet.

Re Item IV

Lack of unity of invention

The separate inventions/groups of invention are:

Invention 1: Claims 1 and 14 completely and claims 10 to 13, 23 to 32 partially.

Nucleic acid sequence encoding a 75kD *Lawsonia intracellularis* protein or a part of said nucleic acid sequence that encodes an immunogenic fragment of said protein said nucleic acid sequence, or said part thereof having at least 90% homology with the nucleic acid sequence as depicted in SEQ ID NO: 1, protein that is at least 90% homologous to SEQ ID NO: 2, live recombinant carrier, host cell, vaccine comprising said nucleic acid, use of said protein in the manufacture of a vaccine and method of preparing said vaccine, diagnostic tests involving said nucleic acid or proteins.

Invention 2: Claims 2 and 15 completely and claims 10 to 13, 23 to 32 partially.

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Nucleic acid sequence encoding a 27kD *Lawsonia intracellularis* protein or a part of said nucleic acid sequence that encodes an immunogenic fragment of said protein said nucleic acid sequence, or said part thereof having at least 90% homology with the nucleic acid sequence as depicted in SEQ ID NO: 3, protein that is at least 90% homologous to SEQ ID NO: 4, live recombinant carrier, host cell, vaccine comprising said nucleic acid, use of said protein in the manufacture of a vaccine and method of preparing said vaccine, diagnostic tests involving said nucleic acid or proteins.

Invention 3: Claims 3 and 16 completely and claims 10 to 13, 23 to 32 partially.

Nucleic acid sequence encoding a 62kD *Lawsonia intracellularis* protein or a part of said nucleic acid sequence that encodes an immunogenic fragment of said protein said nucleic acid sequence, or said part thereof having at least 90% homology with the nucleic acid sequence as depicted in SEQ ID NO: 5, protein that is at least 90% homologous to SEQ ID NO: 6, live recombinant carrier, host cell, vaccine comprising said nucleic acid, use of said protein in the manufacture of a vaccine and method of preparing said vaccine, diagnostic tests involving said nucleic acid or proteins.

Invention 4: Claims 4 and 17 completely and claims 10 to 13, 23 to 32 partially.

Nucleic acid sequence encoding a 57kD Lawsonia intracellularis protein or a part of said nucleic acid sequence that encodes an immunogenic fragment of said protein said nucleic

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acid sequence, or said part thereof having at least 90% homology with the nucleic acid sequence as depicted in SEQ ID NO: 7, protein that is at least 90% homologous to SEQ ID NO: 8, live recombinant carrier, host cell, vaccine comprising said nucleic acid, use of said protein in the manufacture of a vaccine and method of preparing said vaccine, diagnostic tests involving said nucleic acid or proteins.

Invention 5: Claims 5 and 18 completely and claims 10 to 13, 23 to 32 partially.

Nucleic acid sequence encoding a 74kD Lawsonia intracellularis protein or a part of said nucleic acid sequence that encodes an immunogenic fragment of said protein said nucleic acid sequence, or said part thereof having at least 90% homology with the nucleic acid sequence as depicted in SEQ ID NO: 9, protein that is at least 90% homologous to SEQ ID NO: 10, live recombinant carrier, host cell, vaccine comprising said nucleic acid, use of said protein in the manufacture of a vaccine and method of preparing said vaccine, diagnostic tests involving said nucleic acid or proteins.

Invention 6: Claims 6 and 19 completely and claims 10 to 13, 23 to 32 partially. Nucleic acid sequence encoding a 44kD Lawsonia intracellularis protein or a part of said nucleic acid sequence that encodes an immunogenic fragment of said protein said nucleic acid sequence, or said part thereof having at least 90% homology with the nucleic acid sequence as depicted in SEQ ID NO: 11, protein that is at least 90% homologous to SEQ ID NO: 12, live recombinant carrier, host cell, vaccine comprising said nucleic acid, use of said protein in the manufacture of a vaccine and method of preparing said vaccine, diagnostic tests involving said nucleic acid or proteins.

Invention 7: Claims 7 and 20 completely and claims 10 to 13, 23 to 32 partially. Nucleic acid sequence encoding a 43kD Lawsonia intracellularis protein or a part of said nucleic acid sequence that encodes an immunogenic fragment of said protein said nucleic acid sequence, or said part thereof having at least 90% homology with the nucleic acid sequence as depicted in SEQ ID NO: 13, protein that is at least 90% homologous to SEQ ID NO: 14, live recombinant carrier, host cell, vaccine comprising said nucleic acid, use of said protein in the manufacture of a vaccine and method of preparing said vaccine, diagnostic tests involving said nucleic acid or proteins.

Invention 8: Claims 8 and 21 completely and claims 10 to 13, 23 to 32 partially.

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Nucleic acid sequence encoding a 26/31kD Lawsonia intracellularis protein or a part of said nucleic acid sequence that encodes an immunogenic fragment of said protein said nucleic acid sequence, or said part thereof having at least 90% homology with the nucleic acid sequence as depicted in SEQ ID NO: 15, protein that is at least 90% homologous to SEQ ID NO: 16, live recombinant carrier, host cell, vaccine comprising said nucleic acid, use of said protein in the manufacture of a vaccine and method of preparing said vaccine, diagnostic tests involving said nucleic acid or proteins.

Invention 9: Claims 9 and 22 completely and claims 10 to 13, 23 to 32 partially. Nucleic acid sequence encoding a 101kD Lawsonia intracellularis protein or a part of said nucleic acid sequence that encodes an immunogenic fragment of said protein said nucleic acid sequence, or said part thereof having at least 90% homology with the nucleic acid sequence as depicted in SEQ ID NO: 17, protein that is at least 90% homologous to SEQ ID NO: 18, live recombinant carrier, host cell, vaccine comprising said nucleic acid, use of said protein in the manufacture of a vaccine and method of preparing said vaccine, diagnostic tests involving said nucleic acid or proteins.

The general concept of characterizing nucleic acids which encode *Lawsonia intracellularis* proteins as using them in vaccines against *Lawsonia intracellularis* is already known from the prior art document D1: EP-A-1 219 711 (Akzo Nobel N.V.) and D2: WO-A-0 226 250 (Arizona Board of Regents on behalf of the University of Arizona.)

D1 discloses nucleic acid sequences encoding *Lawsonia intracellularis* outer membrane proteins and immunogenic fragments for use as vaccines against *Lawsonia intracellularis*. D2 describes vaccines against proliferative ileitis containing protective immunogenic subunits of *Lawsonia intracellularis*.

Due to the fact that the common unifying concept is known in the state of the art, there appears therefore to be no technical features in common between the different inventions involving different nucleotide and amino acid sequences, that could provide a novel and inventive unifying concept.

Consequently, the requisite unity of invention (Rule 13.1 PCT) therefore

no longer exists inasmuch as a technical relationship involving one or more of the same or corresponding special technical features in the sense of Rule 13.2 PCT does not exist between the subject-matter of the groups of claims.

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Examination of:

Invention 1: Claims 1 and 14 completely and claims 10 to 13, 23 to 32 partially.

Nucleic acid sequence encoding a 75kD Lawsonia intracellularis protein or a part of said nucleic acid sequence that encodes an immunogenic fragment of said protein said nucleic acid sequence, or said part thereof having at least 90% homology with the nucleic acid sequence as depicted in SEQ ID NO: 1, protein that is at least 90% homologous to SEQ ID NO: 2, live recombinant carrier, host cell, vaccine comprising said nucleic acid, use of said protein in the manufacture of a vaccine and method of preparing said vaccine, diagnostic tests involving said nucleic acid or proteins.

- The following documents are referred to in this communication; the numbering will be adhered to in the rest of the procedure:
 - D1: EP-A-1 219 711 (Akzo Nobel N.V.)

D2: WO-A-0 226 250 (Arizona Board of Regents on behalf of the University of Arizona.)

- 2 **NOVELTY** (Art. 33(2) PCT)
- 2.1 In view of the prior art cited, claims 1 and 14 and claims dependent thereon appear to be novel and meet therefore the requirements of Art.33(2) PCT, since

the nucleic and amino acid sequences SEQ ID NOs: 1 and 2 are not disclosed in the state of the art.

3 **INVENTIVE STEP** (Art. 33(3) PCT)

- 3.1 Documents D2 and D3 are considered to represent the most relevant state of the art. D2 discloses nucleic acid sequences encoding *Lawsonia intracellularis* outer membrane proteins and immunogenic fragments for use as vaccines against *Lawsonia intracellularis*. D3 describes vaccines against proliferative ileitis containing protective immunogenic subunits of *Lawsonia intracellularis*.
- The subject-matter of the present application and claims 1 and 14 and claims dependent thereon involve different nucleic acid sequences and their use as immunogenic fragments as vaccines against *Lawsonia intracellularis*.
- 3.3 The problem may be defined as the provision of alternative nucleic acid sequences and immunogenic fragments for use as vaccines against *Lawsonia intracellularis*.
- However due to the fact that the above problem has previously been solved by the subunit vaccines of the state of the art and that there is no evidence in the description that the nucleic or amino acid sequences SEQ ID NOs: 1 and 2 actually solve the problem through initiating an effective protective immune response to *Lawsonia intracellularis*, the subject-matter of claims 1 and 14 cannot be recognized as involving an inventive step according to Article 33(3) PCT.
- Dependent claims 10 to 13, 23 to 32, as far as they are dependent upon claims 1 and 14, do not appear to contain any additional features which, in combination with the features of any claim to which they refer, involve an inventive step.
- In view of the above, the present application does not meet the requirements of Article 33(3) PCT, because the subject-matter of claims 1, 10 to 14, 23 to 32 does

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not involve an inventive step.

For the assessment of the present claims 23 and 24 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

PATENT COOPERATION TREATY

From	the RNATIONAL SEARCHING AUTH	ORITY		WIPO PCT				
To:				PCT				
	see form PCT/ISA/220		INTERNATIO	TEN OPINION OF THE NAL SEARCHING AUTHORITY (PCT Rule 43bis.1)				
			(day/month/year) so	ee form PCT/ISA/210 (second sheet)				
' '	licant's or agent's file reference form PCT/ISA/220		FOR FURTHER See paragraph 2 bel	·				
	national application No. T/EP2005/000562	International filing date (18.01.2005	day/month/year)	Priority date (day/month/year) 22.01.2004				
	national Patent Classification (IPC) or 7K14/195, C12N15/31, C07K16							
, , ,	icant ZO NOBEL N.V.							
2.	 ☑ Box No. IV Lack of unity of Box No. V ☑ Box No. V ☑ Box No. VI Certain docum ☑ Box No. VII Certain defect ☑ Box No. VIII Certain observed FURTHER ACTION If a demand for international prewritten opinion of the Internation 	ment of opinion with regard invention tement under Rule 43bis itations and explanations nents cited in the international appraisons on the internation of all Preliminary examination is a second control of the internation of the internation is a second control of the internation in the internation is a second control of the internation in the internation is a second control of the internation in the internation is a second control of the internation in the internation in the internation is a second control of the internation in the internation in the internation in the internation is a second control of the internation in the internation in the internation is a second control of the internation in the internation in the internation is a second control of the internation in the internation in the internation in the internation is a second control of the internation in the inte	ard to novelty, invention of the state of th	Il usually be considered to be a However, this does not apply where				
3.	written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1 bis(b) that written opinions of this International Searching Authority will not be so considered. If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of malling of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later. For further options, see Form PCT/ISA/220. 3. For further details, see notes to Form PCT/ISA/220.							
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Nam	e and mailing address of the ISA:		Authorized Officer	Set Films.				

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Hix, R

Telephone No. +31 70 340-3898



International application No. PCT/EP2005/000562

	Вох	No. I	Basis of the opinion		
1.			d to the language, this opinion has been established on the basis of the internati ge in which it was filed, unless otherwise indicated under this item.	onal application	in
	t	angua	pinion has been established on the basis of a translation from the original langua age , which is the language of a translation furnished for the purposes of intern Rules 12.3 and 23.1(b)).		wing
2.			d to any nucleotide and/or amino acid sequence disclosed in the international to the claimed invention, this opinion has been established on the basis of:	application and	
	a. typ	e of m	naterial:		
	\boxtimes	a se	equence listing	•	
	. 🗆	table	le(s) related to the sequence listing		•
	b. for	mat of	f material:		
	\boxtimes	in w	vritten format	.`	•
	\boxtimes	in c	omputer readable form	•	
	c. tim	e of fil	ling/furnishing:		
	\boxtimes	cont	tained in the international application as filed.		
	\boxtimes	filed	together with the international application in computer readable form.		
		fum	ished subsequently to this Authority for the purposes of search.		
3.	h	as bed opies	tion, in the case that more than one version or copy of a sequence listing and/or the en filed or furnished, the required statements that the information in the subsequence is identical to that in the application as filed or does not go beyond the application riate, were furnished.	ent or additional	

4. Additional comments:

International application No. PCT/EP2005/000562

_	Во	x No. IV	/ Lack of unity of	inventio	ו				
1.		In resp	oonse to the invitation	n (Form F	CT/ISA/20	6) to pay additional fees, the applicant has:			
			paid additional fee	S.		·			
			paid additional fee	s under pr	otest.				
			not paid additional	fees.					
2.			uthority found that to plicant to pay addition		ment of un	ity of invention is not complied with and cho	se not to invite		
3.	Thi	s Autho	rity considers that th	ne requirer	nent of uni	ty of invention in accordance with Rule 13.1	, 13.2 and 13.3 is		
	□ complied with								
		•	plied with for the fol	lowing res	isons.	•			
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			parate sheet			•	·		
4.	Cor	Consequently, this report has been established in respect of the following parts of the International application:							
	□ all parts.								
		the part	s relating to claims l	Vos. 1, 10	-14, 23-32	•			
	•				٠				
-	Box	x No. V ustrial	Reasoned state applicability; citati	ment und ons and e	er Rule 43 explanation	bis.1(a)(i) with regard to novelty, inventions supporting such statement	ve step or		
1.	Sta	tement							
	Nov	velty (N)		Yes: No:	Claims Claims	1, 10-14, 23-32			
	Inve	entive st	tep (IS)	Yes: No:	Claims ,	1, 10-14, 23-32			
				,					
	Indi	ustrial a	pplicability (IA)	Yes: No:	Claims Claims	1, 10-14, 23-32			

2. Citations and explanations

see separate sheet

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Re Item IV

Lack of unity of invention

The separate inventions/groups of invention are:

Invention 1: Claims 1 and 14 completely and claims 10 to 13, 23 to 32 partially.

Nucleic acid sequence encoding a 75kD *Lawsonia intracellularis* protein or a part of said nucleic acid sequence that encodes an immunogenic fragment of said protein said nucleic acid sequence, or said part thereof having at least 90% homology with the nucleic acid sequence as depicted in SEQ ID NO: 1, protein that is at least 90% homologous to SEQ ID NO: 2, live recombinant carrier, host cell, vaccine comprising said nucleic acid, use of said protein in the manufacture of a vaccine and method of preparing said vaccine, diagnostic tests involving said nucleic acid or proteins.

Invention 2: Claims 2 and 15 completely and claims 10 to 13, 23 to 32 partially.

Nucleic acid sequence encoding a 27kD Lawsonia intracellularis protein or a part of said nucleic acid sequence that encodes an immunogenic fragment of said protein said nucleic acid sequence, or said part thereof having at least 90% homology with the nucleic acid sequence as depicted in SEQ ID NO: 3, protein that is at least 90% homologous to SEQ ID NO: 4, live recombinant carrier, host cell, vaccine comprising said nucleic acid, use of said protein in the manufacture of a vaccine and method of preparing said vaccine, diagnostic tests involving said nucleic acid or proteins.

Invention 3: Claims 3 and 16 completely and claims 10 to 13, 23 to 32 partially. Nucleic acid sequence encoding a 62kD Lawsonia intracellularis protein or a part of said nucleic acid sequence that encodes an immunogenic fragment of said protein said nucleic acid sequence, or said part thereof having at least 90% homology with the nucleic acid sequence as depicted in SEQ ID NO: 5, protein that is at least 90% homologous to SEQ ID NO: 6, live recombinant carrier, host cell, vaccine comprising said nucleic acid, use of said protein in the manufacture of a vaccine and method of preparing said vaccine, diagnostic tests involving said nucleic acid or proteins.

Invention 4: Claims 4 and 17 completely and claims 10 to 13, 23 to 32 partially.

Nucleic acid sequence encoding a 57kD Lawsonia intracellularis protein or a part of said nucleic acid sequence that encodes an immunogenic fragment of said protein said nucleic

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acid sequence, or said part thereof having at least 90% homology with the nucleic acid sequence as depicted in SEQ ID NO: 7, protein that is at least 90% homologous to SEQ ID NO: 8, live recombinant carrier, host cell, vaccine comprising said nucleic acid, use of said protein in the manufacture of a vaccine and method of preparing said vaccine, diagnostic tests involving said nucleic acid or proteins.

Invention 5: Claims 5 and 18 completely and claims 10 to 13. 23 to 32 partially. Nucleic acid sequence encoding a 74kD Lawsonia intracellularis protein or a part of said nucleic acid sequence that encodes an immunogenic fragment of said protein said nucleic acid sequence, or said part thereof having at least 90% homology with the nucleic acid sequence as depicted in SEQ ID NO: 9, protein that is at least 90% homologous to SEQ ID NO: 10, live recombinant carrier, host cell, vaccine comprising said nucleic acid, use of said protein in the manufacture of a vaccine and method of preparing said vaccine, diagnostic tests involving said nucleic acid or proteins.

Invention 6: Claims 6 and 19 completely and claims 10 to 13, 23 to 32 partially. Nucleic acid sequence encoding a 44kD Lawsonia intracellularis protein or a part of said nucleic acid sequence that encodes an immunogenic fragment of said protein said nucleic acid sequence, or said part thereof having at least 90% homology with the nucleic acid sequence as depicted in SEQ ID NO: 11, protein that is at least 90% homologous to SEQ ID NO: 12, live recombinant carrier, host cell, vaccine comprising said nucleic acid, use of said protein in the manufacture of a vaccine and method of preparing said vaccine, diagnostic tests involving said nucleic acid or proteins.

Invention 7: Claims 7 and 20 completely and claims 10 to 13, 23 to 32 partially. Nucleic acid sequence encoding a 43kD Lawsonia intracellularis protein or a part of said nucleic acid sequence that encodes an immunogenic fragment of said protein said nucleic acid sequence, or said part thereof having at least 90% homology with the nucleic acid sequence as depicted in SEQ ID NO: 13, protein that is at least 90% homologous to SEQ ID NO: 14, live recombinant carrier, host cell, vaccine comprising said nucleic acid, use of said protein in the manufacture of a vaccine and method of preparing said vaccine, diagnostic tests involving said nucleic acid or proteins.

Invention 8: Claims 8 and 21 completely and claims 10 to 13, 23 to 32 partially.

Nucleic acid sequence encoding a 26/31kD *Lawsonia intracellularis* protein or a part of said nucleic acid sequence that encodes an immunogenic fragment of said protein said nucleic acid sequence, or said part thereof having at least 90% homology with the nucleic acid sequence as depicted in SEQ ID NO: 15, protein that is at least 90% homologous to SEQ ID NO: 16, live recombinant carrier, host cell, vaccine comprising said nucleic acid, use of said protein in the manufacture of a vaccine and method of preparing said vaccine, diagnostic tests involving said nucleic acid or proteins.

Invention 9: Claims 9 and 22 completely and claims 10 to 13, 23 to 32 partially. Nucleic acid sequence encoding a 101kD Lawsonia intracellularis protein or a part of said nucleic acid sequence that encodes an immunogenic fragment of said protein said nucleic acid sequence, or said part thereof having at least 90% homology with the nucleic acid sequence as depicted in SEQ ID NO: 17, protein that is at least 90% homologous to SEQ ID NO: 18, live recombinant carrier, host cell, vaccine comprising said nucleic acid, use of said protein in the manufacture of a vaccine and method of preparing said vaccine, diagnostic tests involving said nucleic acid or proteins.

The general concept of characterizing nucleic acids which encode *Lawsonia intracellularis* proteins as using them in vaccines against *Lawsonia intracellularis* is already known from the prior art document D1: EP-A-1 219 711 (Akzo Nobel N.V.) and D2: WO-A-0 226 250 (Arizona Board of Regents on behalf of the University of Arizona.)

D1 discloses nucleic acid sequences encoding *Lawsonia intracellularis* outer membrane proteins and immunogenic fragments for use as vaccines against *Lawsonia intracellularis*. D2 describes vaccines against proliferative ileitis containing protective immunogenic subunits of *Lawsonia intracellularis*.

Due to the fact that the common unifying concept is known in the state of the art, there appears therefore to be no technical features in common between the different inventions involving different nucleotide and amino acid sequences, that could provide a novel and inventive unifying concept.

Consequently, the requisite unity of invention (Rule 13.1 PCT) therefore

no longer exists inasmuch as a technical relationship involving one or more of the same or corresponding special technical features in the sense of Rule 13.2 PCT does not exist between the subject-matter of the groups of claims.

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Examination of:

Invention 1: Claims 1 and 14 completely and claims 10 to 13, 23 to 32 partially. Nucleic acid sequence encoding a 75kD Lawsonia intracellularis protein or a part of said nucleic acid sequence that encodes an immunogenic fragment of said protein said nucleic acid sequence, or said part thereof having at least 90% homology with the nucleic acid sequence as depicted in SEQ ID NO: 1, protein that is at least 90% homologous to SEQ ID NO: 2, live recombinant carrier, host cell, vaccine comprising said nucleic acid, use of said protein in the manufacture of a vaccine and method of preparing said vaccine, diagnostic tests involving said nucleic acid or proteins.

- The following **documents** are referred to in this communication; the numbering will be adhered to in the rest of the procedure:
 - D1: EP-A-1 219 711 (Akzo Nobel N.V.)
- D2: WO-A-0 226 250 (Arizona Board of Regents on behalf of the University of Arizona.)
- 2 **NOVELTY** (Art. 33(2) PCT)
- 2.1 In view of the prior art cited, claims 1 and 14 and claims dependent thereon appear to be novel and meet therefore the requirements of Art.33(2) PCT, since

the nucleic and amino acid sequences SEQ ID NOs: 1 and 2 are not disclosed in the state of the art.

3 INVENTIVE STEP (Art. 33(3) PCT)

- 3.1 Documents D2 and D3 are considered to represent the most relevant state of the art. D2 discloses nucleic acid sequences encoding *Lawsonia intracellularis* outer membrane proteins and immunogenic fragments for use as vaccines against *Lawsonia intracellularis*. D3 describes vaccines against proliferative ileitis containing protective immunogenic subunits of *Lawsonia intracellularis*.
- The subject-matter of the present application and claims 1 and 14 and claims dependent thereon involve different nucleic acid sequences and their use as immunogenic fragments as vaccines against *Lawsonia intracellularis*.
- 3.3 The problem may be defined as the provision of alternative nucleic acid sequences and immunogenic fragments for use as vaccines against *Lawsonia intracellularis*.
- However due to the fact that the above problem has previously been solved by the subunit vaccines of the state of the art and that there is no evidence in the description that the nucleic or amino acid sequences SEQ ID NOs: 1 and 2 actually solve the problem through initiating an effective protective immune response to *Lawsonia intracellularis*, the subject-matter of claims 1 and 14 cannot be recognized as involving an inventive step according to Article 33(3) PCT.
- Dependent claims 10 to 13, 23 to 32, as far as they are dependent upon claims 1 and 14, do not appear to contain any additional features which, in combination with the features of any claim to which they refer, involve an inventive step.
- In view of the above, the present application does not meet the requirements of Article 33(3) PCT, because the subject-matter of claims 1, 10 to 14, 23 to 32 does

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not involve an inventive step.

For the assessment of the present claims 23 and 24 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.